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Lrig1 expression identifies airway basal cells with high proliferative capacity and restricts lung squamous cell carcinoma growth

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Shareable abstract (@ERSpublications)
LRIG1 is lost in development of squamous cell lung cancers. This study shows that LRIG1 marks basal airway progenitor cells with high proliferative potential and regulates progression of pre-invasive squamous cell lung cancer. https://bit.ly/3AbPtY3

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Abstract

Background Lung squamous cell carcinoma (LUSC) accounts for a significant proportion of cancer deaths worldwide, and is preceded by the appearance of progressively disorganised pre-invasive lesions in the airway epithelium. Yet the biological mechanisms underlying progression of pre-invasive lesions into invasive LUSC are not fully understood. *LRIG1* (leucine-rich repeats and immunoglobulin-like domains 1) is downregulated in pre-invasive airway lesions and invasive LUSC tumours and this correlates with decreased lung cancer patient survival.

Methods and results Using an *Lrig1* knock-in reporter mouse and human airway epithelial cells collected at bronchoscopy, we show that during homeostasis LRIG1 is heterogeneously expressed in the airway epithelium. In basal airway epithelial cells, the suspected cell of origin of LUSC, LRIG1 identifies a subpopulation of progenitor cells with higher *in vitro* proliferative and self-renewal potential in both the mouse and human. Using the N-nitroso-tris-chloroethylurea (NTCU)-induced murine model of LUSC, we find that *Lrig1* loss-of-function leads to abnormally high cell proliferation during the earliest stages of pre-invasive disease and to the formation of significantly larger invasive tumours, suggesting accelerated disease progression.

Conclusion Together, our findings identify LRIG1 as a marker of basal airway progenitor cells with high proliferative potential and as a regulator of pre-invasive lung cancer progression. This work highlights the clinical relevance of LRIG1 and the potential of the NTCU-induced LUSC model for functional assessment of candidate tumour suppressors and oncogenes.